18. (Amended) The method of claim 4, wherein said statin is Compactin, Atorvastatin, Lovastatin, Pravastatin, Fluvastatin, Mevastatin, Cerivastatin, Rosuvastatin or Simvastatin.

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19. (Amended) The method of claim 4, wherein said statin is Atorvastatin.

20. (Amended) The method of claim 4, wherein said statin, or said functionally or structurally equivalent molecule, has no lipid-lowering effect.

21. (Amended) The method of claim 4, wherein the statin, or a functionally or structurally equivalent molecule, is administered in the absence of any other immunosuppressive agents.

22. (Amended) The method of claim 4, wherein said amount is comprised between 10 and 80 mg per day.

23. (Amended) The method of claim 4, wherein said amount is comprised between 20 and 40 mg per day.

24. (Amended) The method of claim 4, wherein said administration comprises intralesional, intraperitoneal, intramuscular or intravenous injection; infusion; or topical, nasal, oral, ocular or otic delivery.

25. (Amended) The method of claim 4, wherein said administration is made daily.

26. (Amended) The method of claim 4, wherein the immunosuppression or anti-inflammatory effect is the result of repression of T lymphocyte activation.

The cancellation of and/or amendments to the claims are being made solely to expedite prosecution of this application. Amendments have been made to make the dependent claims having previous multiple dependencies dependent on claim 4. Applicant reserves the option to further prosecute the same or similar claims in this or in another patent application. No new matter is added. *After entry of this amendment, claims 4-6, 11-12, 16-26, 29-30 and 93 are in the case.*

Pursuant to 37 CFR 1.121(c)(1)(ii), a marked up version of the claims showing the changes made appears as Appendix A of this Amendment.

RESPONSE TO RESTRICTION REQUIREMENT:

The Examiner has required restriction of the claims in this application to one of the following inventions:

I. claims 1, 2, 5-7, 10-11, 16-26 (in part) and 12 (drawn to a method to achieve MHC-class II mediated immunomodulation in a mammal suffering from automimmune diseases such as diabetes, classified in class 514, subclass 311, 423, 460, and 510);

II. claims 3, 5-7, 10-11, 16-26 (in part) and 12 (drawn to a method to achieve MHC-class II mediated anti-inflammatory effect in a mammal suffering from automimmune diseases such as diabetes, classified in class 514, subclass 311, 423, 460, and 510);

III. claims 4, 5-7, 10-11, 16-26 (in part) and 12 (drawn to a method to achieve CD40 mediated anti-inflammatory effect in a mammal suffering from automimmune diseases such as diabetes, classified in class 514, subclass 311, 423, 460, and 510);

IV. claims 1, 2, 5-7, 10-11, 16-26 (in part) and 13-14 (drawn to a method to achieve MHC-class II mediated immunomodulation in a mammal under treatment in preparation of an organ or tissue transplantation, classified in class 514, subclass 311, 423, 460, and 510);

V. claims 3, 5-7, 10-11, 16-26 (in part) and 13-14 (drawn to a method to achieve MHC-class mediated anti-inflammatory effect in a mammal under treatment in preparation of an organ or tissue transplantation, classified in class 514, subclass 311, 423, 460, 510);

VI. claims 4, 5-7, 10-11, 16-26 (in part) and 13-14 (drawn to a method to achieve CD40 mediated anti-inflammatory effect in a mammal under treatment in preparation of an organ or tissue transplantation, classified in class 514, subclass 311, 423, 460, and 510);

VII. claims 1-2, 5-7, 10-11, 16-26 (in part) and 15 (drawn to a method to achieve MHC-class II mediated immunomodulation in a mammal suffering from psoriasis or inflammation, classified in class 514, subclass 311, 423, 460, and 510);

VIII. claims 3, 5-7, 10-11, 16-26 (in part) and 15 (drawn to a method to achieve MHC-class II mediated anti-inflammatory effect in a mammal suffering from psoriasis, classified in class 514, subclass 311, 423, 460, and 510);

IX. claims 4, 5-7, 10-11, 16-26 (in part) and 15 (drawn to a method to achieve CD40 mediated anti-inflammatory effect in a mammal suffering from psoriasis, classified in class 514, subclass 311, 423, 460, and 510);

X. claims 27-28 (drawn to a method for identifying molecules that inhibit IFN-induced CIITA expression, classified in class 435, subclass 1+);

XI. claims 29-30 (drawn to a method for identifying molecules that inhibit CD40 expression, classified in class 435, sublcass 1+);

XII. claims 31-33, 36-46 (drawn to a method of treating a patient afflicted with an autoimmune disease with HMG-CoA reductase inhibitor, classified in class 514, subclass 311, 423, 460, and 510);

XIII. claims 34-35 (drawn to a method of treating a patient in preparation for organ transplantation with a compound with HMG-CoA reductase inhibition and MHC Class II expression, classified in class 514, subclass 311, 423, 460, and 510);

XIV. claims 47-48, 60-63 (drawn to use of a statin to treat immuno-inflammatory disease, classified in class 514, subclass 311, 423, 460, and 510);

XV. claims 49 and 68-75 (drawn to a method of preventing or treating tissue or organ rejection with a compound capable in inhibiting IFN-γ inducible MHC class II expression and/or CD40 expression, classified in class 514, subclass 1+);

XVI. claims 50-59 (drawn to a method of treating a tissue graft, classified in class 514, subclass 311, 423, 460, and 510);

XVII. claims 64-67 (drawn to a kit, classified in class 424, subclass 400+);

XVIII. claims 76-84 (drawn to a method of treating an inflammatory disorder with a compound capable in inhibiting IFN-γ inducible MHC class II expression and/or CD40 expression, classified in class 514, subclass 311, 423, 460, and 510);

XIX. claims 85-92 (drawn to use of a statin to treat inflammatory skin disorder, classified in class 514, subclass 311, 423, 460, and 510); and

XX. claim 93 (drawn to use of a statin to treat inflammatory ocular disorder, classified in class 514, subclass 311, 423, 460, and 510.)

In response, Applicant hereby elects, with traverse, the invention of Group III, encompassed by non-cancelled claims 4-6, 11-12, and 16-26, as amended.

Applicant respectfully submits that the remaining non-cancelled claims, *i.e.,* claims 4-6, 11-12, and 16-26, 29-30 and 93 (in Groups III, VI, IX, XI and XX, respectively) can properly be examined as one group.

These claims, as amended, are drawn to methods of achieving CD40-mediated anti-immuno-inflammation, wherein at least one statin (or a functional or structural equivalent), is administered in an amount effective to modulate CD40 expression. As noted in Applicant's specification, the immune response can become a cause of disease or other undesirable conditions if activated, *e.g.,* autoimmune diseases such as type I diabetes, multiple sclerosis and rheumatoid arthritis, tissue/organ graft rejection, and psoriasis. Inappropriate or undesired immune response in cases like these present a clinical need for immunosuppression. Such conditions often involve the common step of lymphocyte activation.

CD40 and CD40L trigger lymphocyte activation. For example, activation of atheroma associated cells (*e.g.,* macrophages, endothelial cells and smooth muscle cells) via CD40 signaling has been shown to induce inflammatory responses with adhesion molecule expression, secretion of pro-inflammatory cytokines, tissue factor and chemokines.

The inventor found that CD40-mediated anti immuno-inflammatory effect in mammals in need of such treatment may be achieved by statin administration, in an amount effective to modulate CD40 expression, *e.g.,* inducible expression of CD40, most preferably IFN-γ induced CD40 expression. Accordingly, the effect of reduced CD40 expression is reduced lymphocyte activation and, hence, reduced immunoinflammation. This has practical clinical applications including diseases where aberrant activation of CD4 T lymphocytes are implicated, like autoimmune diseases including type I diabetes, psoriasis, inflammatory ocular disorder, and other chronic inflammatory diseases.

In view of the above comments, therefore, *at least* Groups III, VI, IX and XX may be examined together, and without any undue burden on the Examiner.

With respect to Group XI – claims 29 and 30 – Applicant further submits that these claims may be properly included in a single group for examination. These claims are directed to identifying molecules that inhibit induced CD40 expression (such as may be useful in the methods of Groups III, VI, IX and XX); as such, a single search of the prior art is possible and would not require any additional work on the Examiner's part.

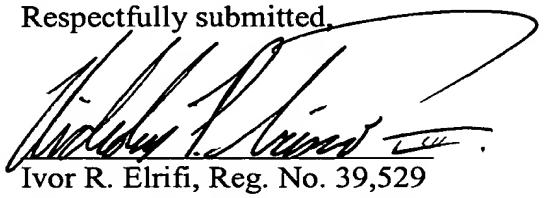
SUMMARY

In view of the above comments and amendments, Applicant respectfully requests that pending claims 4-6, 11-12, and 16-26, 29-30 and 93 (in Groups III, VI, IX, XI and XX, respectively) currently in the case may be examined as a single group.

If a telephone conversation with Applicant's attorney would help expedite the prosecution of this application, the Examiner is invited to call Applicants' attorney at (617) 542-6000.

Please apply any charges not covered, or any credits, to Deposit Account 50-0311 (Reference No. 23135-501CIP).

Respectfully submitted,



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